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<120> Test system for the development of therapeutic agents,
in particular active compounds for the treatment of
osteoporosis

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<304> 1995

<305> 27 (1)

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<304> 1998

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Cys	Leu	Ser	Ala	Leu	Trp	Tyr	Asn	His	Glu	Gln	Cys	Cys	Trp	Gly	Ser	165	170	175	
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Phe	Leu	Asp	Ala	Lys	Glu	Glu	Phe	Glu	Phe	Thr	His	Thr	Thr	Leu	Ala	645	650	655
Ala	Asp	Val	Met	Arg	Pro	Arg	Arg	Asn	Asp	Pro	Pro	Leu	Ala	Val	Leu	660	665	670
Thr	Gln	Asp	Asn	Met	Thr	Val	Asp	Asp	Ile	Glu	Asn	Met	Ile	Asn	Glu	675	680	685
Thr	Ser	Tyr	Asn	Gly	Phe	Pro	Val	Ile	Met	Ser	Lys	Glu	Ser	Gln	Arg	690	695	700

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ggg gca ccg atc gga gga gtt ctt ttt agc ttg gag gag gtt agc tat	1227
Gly Ala Pro Ile Gly Gly Val Leu Phe Ser Leu Glu Glu Val Ser Tyr	
270 275 280	
tat ttt cct ctc aaa act tta tgg aga tca ttt ttt gct gct ttg gtg	1275
Tyr Phe Pro Leu Lys Thr Leu Trp Arg Ser Phe Phe Ala Ala Leu Val	
285 290 295 300	
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Ala Ala Phe Val Leu Arg Ser Ile Asn Pro Phe Gly Asn Ser Arg Leu	
305 310 315	
gtc ctc ttt tat gtg gag tat cat aca cca tgg tac ctt ttt gaa ctg	1371
Val Leu Phe Tyr Val Glu Tyr His Thr Pro Trp Tyr Leu Phe Glu Leu	
320 325 330	
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Phe Pro Phe Ile Leu Leu Gly Val Phe Gly Gly Leu Trp Gly Ala Phe	
335 340 345	
ttt att agg gca aat att gcc tgg tgt cgt cga cgc aag tcc acc aaa	1467
Phe Ile Arg Ala Asn Ile Ala Trp Cys Arg Arg Arg Lys Ser Thr Lys	
350 355 360	
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Phe Gly Lys Tyr Pro Val Leu Glu Val Ile Ile Val Ala Ala Ile Thr	
365 370 375 380	
gct gtg ata gcc ttc ccc aac cca tac aca agg ctc aac acc agt gaa	1563
Ala Val Ile Ala Phe Pro Asn Pro Tyr Thr Arg Leu Asn Thr Ser Glu	
385 390 395	
ctg att aaa gag ctg ttt aca gat tgt ggg ccg ttg gaa tcc tcc tct	1611
Leu Ile Lys Glu Leu Phe Thr Asp Cys Gly Pro Leu Glu Ser Ser Ser	
400 405 410	
ctc tgt gac tac aga aat gac atg aat gcc agt aaa att gtt gac gat	1659
Leu Cys Asp Tyr Arg Asn Asp Met Asn Ala Ser Lys Ile Val Asp Asp	
415 420 425	
att cct gac cgt cca gca ggc gtt gga gta tat tca gct atc tgg cag	1707
Ile Pro Asp Arg Pro Ala Gly Val Gly Val Tyr Ser Ala Ile Trp Gln	
430 435 440	
ttg tgc cta gcg ctc ata ttt aaa ata ata atg aca gta ttc act ttt	1755
Leu Cys Leu Ala Leu Ile Phe Lys Ile Ile Met Thr Val Phe Thr Phe	
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ggt atc aag gtc ccg tca ggc ttg ttt atc ccc agc atg gcc att gga	1803
Gly Ile Lys Val Pro Ser Gly Leu Phe Ile Pro Ser Met Ala Ile Gly	
465 470 475	
gcc att gca ggg aga att gtg ggg atc gct gtg gag cag ctt gcc tac	1851
Ala Ile Ala Gly Arg Ile Val Gly Ile Ala Val Glu Gln Leu Ala Tyr	
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Tyr His His Asp Trp Phe Ile Phe Lys Glu Trp Cys Glu Val Gly Ala	
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Asp Cys Ile Thr Pro Gly Leu Tyr Ala Met Val Gly Ala Ala Ala Cys	
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Leu Gly Gly Val Thr Arg Met Thr Val Ser Leu Val Val Ile Val Phe	
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gaa ctt act gga ggc ttg gaa tat att gtt cct ctt atg gct gca gta	2043
Glu Leu Thr Gly Gly Leu Glu Tyr Ile Val Pro Leu Met Ala Ala Val	
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Met Thr Ser Lys Trp Val Gly Asp Ala Phe Gly Arg Glu Gly Ile Tyr	
560 565 570	
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Glu Ala His Ile Arg Leu Asn Gly Tyr Pro Phe Leu Asp Ala Lys Glu	
575 580 585	
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Glu Phe Thr His Thr Thr Leu Ala Ala Asp Val Met Arg Pro Arg Arg	
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Ser Asp Pro Pro Leu Ala Val Leu Thr Gln Asp Asn Met Thr Val Asp	
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gac ata gaa aac atg att aat gaa acc agc tat aat ggc ttt cct gtt	2283
Asp Ile Glu Asn Met Ile Asn Glu Thr Ser Tyr Asn Gly Phe Pro Val	
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Ile Met Ser Lys Glu Ser Gln Arg Leu Val Gly Phe Ala Leu Arg Arg	
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gac ctg act att gca ata gaa agt gcc aga aaa aaa caa gaa ggg att	2379
Asp Leu Thr Ile Ala Ile Glu Ser Ala Arg Lys Lys Gln Glu Gly Ile	
655 660 665	
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Val Gly Ser Ser Arg Val Cys Phe Ala Gln His Thr Pro Ser Leu Pro	
670 675 680	

gca gaa agt cca cgg cca tta aaa ctg aga agc atc ctt gac atg agc 2475
 Ala Glu Ser Pro Arg Pro Leu Lys Leu Arg Ser Ile Leu Asp Met Ser
 685 690 695 700

cct ttt aca gtg aca gac cac acc cca atg gag att gtg gta gac atc 2523
 Pro Phe Thr Val Thr Asp His Thr Pro Met Glu Ile Val Val Asp Ile
 705 710 715

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 Phe Arg Lys Leu Gly Leu Arg Gln Cys Leu Val Thr His Asn Gly Arg
 720 725 730

ctc ctt ggc att ata aca aaa aaa gat atc ctc cgt cat atg gcc cag 2619
 Leu Leu Gly Ile Ile Thr Lys Lys Asp Ile Leu Arg His Met Ala Gln
 735 740 745

acg gca aac caa gac ccc gct tca ata atg ttc aac tga gtcctgtaga 2668
 Thr Ala Asn Gln Asp Pro Ala Ser Ile Met Phe Asn
 750 755 760

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 35 40 45
 Ile Asn Ser Lys Lys Lys Glu Ser Ala Trp Glu Met Thr Lys Ser Leu
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 Tyr Asp Ala Trp Ser Gly Trp Leu Val Val Thr Leu Thr Gly Leu Ala
 65 70 75 80
 Ser Gly Ala Leu Ala Gly Leu Ile Asp Ile Ala Ala Asp Trp Met Thr
 85 90 95
 Asp Leu Lys Glu Gly Ile Cys Leu Ser Ala Leu Trp Tyr Asn His Glu
 100 105 110
 Gln Cys Cys Trp Gly Ser Asn Glu Thr Thr Phe Glu Glu Arg Asp Lys
 115 120 125
 Cys Pro Gln Trp Lys Thr Trp Ala Glu Leu Ile Ile Gly Gln Ala Glu
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 Gly Pro Gly Ser Tyr Ile Met Asn Tyr Ile Met Tyr Ile Phe Trp Ala
 145 150 155 160
 Leu Ser Phe Ala Phe Leu Ala Val Ser Leu Val Lys Val Phe Ala Pro
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 Tyr Ala Cys Gly Ser Gly Ile Pro Glu Ile Lys Thr Ile Leu Ser Gly
 180 185 190
 Phe Ile Ile Arg Gly Tyr Leu Gly Lys Trp Thr Leu Met Ile Lys Thr
 195 200 205
 Ile Thr Leu Val Leu Ala Val Ala Ser Gly Leu Ser Leu Gly Lys Glu
 210 215 220

Gly	Pro	Leu	Val	His	Val	Ala	Cys	Cys	Cys	Gly	Asn	Ile	Phe	Ser	Tyr	225	230	235	240
Leu	Phe	Pro	Lys	Tyr	Ser	Thr	Asn	Glu	Ala	Lys	Lys	Arg	Glu	Val	Leu	245	250	255	
Ser	Ala	Ala	Ser	Ala	Ala	Gly	Val	Ser	Val	Ala	Phe	Gly	Ala	Pro	Ile	260	265	270	
Gly	Gly	Val	Leu	Phe	Ser	Leu	Glu	Glu	Val	Ser	Tyr	Tyr	Phe	Pro	Leu	275	280	285	
Lys	Thr	Leu	Trp	Arg	Ser	Phe	Phe	Ala	Ala	Leu	Val	Ala	Ala	Phe	Val	290	295	300	
Leu	Arg	Ser	Ile	Asn	Pro	Phe	Gly	Asn	Ser	Arg	Leu	Val	Leu	Phe	Tyr	305	310	315	320
Val	Glu	Tyr	His	Thr	Pro	Trp	Tyr	Leu	Phe	Glu	Leu	Phe	Pro	Phe	Ile	325	330	335	
Leu	Leu	Gly	Val	Phe	Gly	Gly	Leu	Trp	Gly	Ala	Phe	Phe	Ile	Arg	Ala	340	345	350	
Asn	Ile	Ala	Trp	Cys	Arg	Arg	Arg	Lys	Ser	Thr	Lys	Phe	Gly	Lys	Tyr	355	360	365	
Pro	Val	Leu	Glu	Val	Ile	Ile	Val	Ala	Ala	Ile	Thr	Ala	Val	Ile	Ala	370	375	380	
Phe	Pro	Asn	Pro	Tyr	Thr	Arg	Leu	Asn	Thr	Ser	Glu	Leu	Ile	Lys	Glu	385	390	395	400
Leu	Phe	Thr	Asp	Cys	Gly	Pro	Leu	Glu	Ser	Ser	Ser	Leu	Cys	Asp	Tyr	405	410	415	
Arg	Asn	Asp	Met	Asn	Ala	Ser	Lys	Ile	Val	Asp	Asp	Ile	Pro	Asp	Arg	420	425	430	
Pro	Ala	Gly	Val	Gly	Val	Tyr	Ser	Ala	Ile	Trp	Gln	Leu	Cys	Leu	Ala	435	440	445	
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Pro	Ser	Gly	Leu	Phe	Ile	Pro	Ser	Met	Ala	Ile	Gly	Ala	Ile	Ala	Gly	465	470	475	480
Arg	Ile	Val	Gly	Ile	Ala	Val	Glu	Gln	Leu	Ala	Tyr	Tyr	His	His	Asp	485	490	495	
Trp	Phe	Ile	Phe	Lys	Glu	Trp	Cys	Glu	Val	Gly	Ala	Asp	Cys	Ile	Thr	500	505	510	
Pro	Gly	Leu	Tyr	Ala	Met	Val	Gly	Ala	Ala	Ala	Cys	Leu	Gly	Gly	Val	515	520	525	
Thr	Arg	Met	Thr	Val	Ser	Leu	Val	Val	Ile	Val	Phe	Glu	Leu	Thr	Gly	530	535	540	
Gly	Leu	Glu	Tyr	Ile	Val	Pro	Leu	Met	Ala	Ala	Val	Met	Thr	Ser	Lys	545	550	555	560
Trp	Val	Gly	Asp	Ala	Phe	Gly	Arg	Glu	Gly	Ile	Tyr	Glu	Ala	His	Ile	565	570	575	
Arg	Leu	Asn	Gly	Tyr	Pro	Phe	Leu	Asp	Ala	Lys	Glu	Glu	Phe	Thr	His	580	585	590	
Thr	Thr	Leu	Ala	Ala	Asp	Val	Met	Arg	Pro	Arg	Arg	Ser	Asp	Pro	Pro	595	600	605	
Leu	Ala	Val	Leu	Thr	Gln	Asp	Asn	Met	Thr	Val	Asp	Asp	Ile	Glu	Asn	610	615	620	
Met	Ile	Asn	Glu	Thr	Ser	Tyr	Asn	Gly	Phe	Pro	Val	Ile	Met	Ser	Lys	625	630	635	640
Glu	Ser	Gln	Arg	Leu	Val	Gly	Phe	Ala	Leu	Arg	Arg	Asp	Leu	Thr	Ile	645	650	655	
Ala	Ile	Glu	Ser	Ala	Arg	Lys	Lys	Gln	Glu	Gly	Ile	Val	Gly	Ser	Ser	660	665	670	
Arg	Val	Cys	Phe	Ala	Gln	His	Thr	Pro	Ser	Leu	Pro	Ala	Glu	Ser	Pro	675	680	685	

Arg Pro Leu Lys Leu Arg Ser Ile Leu Asp Met Ser Pro Phe Thr Val
 690 695 700
 Thr Asp His Thr Pro Met Glu Ile Val Val Asp Ile Phe Arg Lys Leu
 705 710 715 720
 Gly Leu Arg Gln Cys Leu Val Thr His Asn Gly Arg Leu Leu Gly Ile
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 Asp Leu Lys Glu Gly Val Cys Leu Ser Ala Phe Trp Tyr Ser His Glu
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 Gln Cys Cys Trp Thr Ser Asn Glu Thr Thr Phe Glu Asp Arg Asp Lys
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 tgt ccc ctg tgg cag aaa tgg tgc gag ctg ctg gtg aat cag tca gag 200
 Cys Pro Leu Trp Gln Lys Trp Ser Glu Leu Leu Val Asn Gln Ser Glu
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 Gly Ala Ser Ala Tyr Ile Leu Asn Tyr Leu Met Tyr Ile Leu Trp Ala
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 ctg ctg ttt gca ttt ttg gct gtc tcc ctg gtg cgt gta ttt gca cca 296
 Leu Leu Phe Ala Phe Leu Ala Val Ser Leu Val Arg Val Phe Ala Pro
 70 75 80
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 Tyr Ala Cys Gly Ser Gly Ile Pro Glu Ile Lys Thr Ile Leu Ser Gly
 85 90 95

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Phe Ile Ile Arg Gly Tyr Leu Gly Lys Trp Thr Leu Leu Ile Lys Thr	
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Val Thr Leu Val Leu Val Val Ser Ser Gly Leu Ser Leu Gly Lys Glu	
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Gly Pro Leu Val His Val Ala Cys Cys Cys Gly Asn Phe Phe Ser Ser	
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Leu Phe Ser Lys Tyr Ser Lys Asn Glu Gly Lys Arg Arg Glu Val Leu	
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Ser Ala Ala Ala Ala Ala Gly Val Ser Val Ala Phe Gly Ala Pro Ile	
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Gly Gly Val Leu Phe Ser Leu Glu Glu Val Ser Tyr Tyr Phe Pro Leu	
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Lys Thr Leu Trp Arg Ser Phe Phe Ala Ala Leu Val Ala Ala Phe Thr	
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Leu Arg Ser Ile Asn Pro Phe Gly Asn Ser Arg Leu Val Leu Phe Tyr	
215 220 225	
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Val Glu Tyr His Thr Pro Trp Tyr Met Ala Glu Leu Phe Pro Phe Ile	
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Leu Leu Gly Val Phe Gly Gly Leu Trp Gly Thr Leu Phe Ile Arg Cys	
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Asn Ile Ala Trp Cys Arg Arg Arg Lys Thr Thr Arg Leu Gly Lys Tyr	
260 265 270	
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Pro Val Leu Glu Val Ile Val Val Thr Ala Ile Thr Ala Ile Ile Ala	
275 280 285 290	
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Tyr Pro Asn Pro Tyr Thr Arg Gln Ser Thr Ser Glu Leu Ile Ser Glu	
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Leu Phe Asn Asp Cys Gly Ala Leu Glu Ser Ser Gln Leu Cys Asp Tyr	
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Ile Asn Asp Pro Asn Met Thr Arg Pro Val Asp Asp Ile Pro Asp Arg	
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Pro Ala Gly Val Gly Val Tyr Thr Ala Met Trp Gln Leu Ala Leu Ala	
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Leu Ile Phe Lys Ile Val Val Thr Ile Phe Thr Phe Gly Met Lys Ile	
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Pro Ser Gly Leu Phe Ile Pro Ser Met Ala Val Gly Ala Ile Ala Gly	
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Arg Met Val Gly Ile Gly Val Glu Gln Leu Ala Tyr His His His Asp	
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Trp Ile Ile Phe Arg Asn Trp Cys Arg Pro Gly Ala Asp Cys Val Thr	
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Gly Leu Glu Tyr Ile Val Pro Leu Met Ala Ala Ala Val Thr Ser Lys	
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Trp Val Ala Asp Ala Phe Gly Lys Glu Gly Ile Tyr Glu Ala His Ile	
470 475 480	
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His Leu Asn Gly Tyr Pro Phe Leu Asp Val Lys Asp Glu Phe Thr His	
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Arg Thr Leu Ala Thr Asp Val Met Arg Pro Arg Arg Gly Glu Pro Pro	
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Leu Ile Lys Glu Thr Asp Tyr Asn Gly Phe Pro Val Val Val Ser Arg	
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Asp Ser Glu Arg Leu Ile Gly Phe Ala Gln Arg Arg Glu Leu Ile Leu
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Ile Met Tyr Phe Thr Glu Glu Pro Pro Glu Leu Pro Ala Asn Ser Pro
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630 635 640

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Asp	Lys	Cys	Pro	Leu	Trp	Gln	Lys	Trp	Ser	Glu	Leu	Leu	Val	Asn	Gln
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Ser	Glu	Gly	Ala	Ser	Ala	Tyr	Ile	Leu	Asn	Tyr	Leu	Met	Tyr	Ile	Leu
	50					55					60				
Trp	Ala	Leu	Leu	Phe	Ala	Phe	Leu	Ala	Val	Ser	Leu	Val	Arg	Val	Phe
65					70					75					80
Ala	Pro	Tyr	Ala	Cys	Gly	Ser	Gly	Ile	Pro	Glu	Ile	Lys	Thr	Ile	Leu
				85					90					95	
Ser	Gly	Phe	Ile	Ile	Arg	Gly	Tyr	Leu	Gly	Lys	Trp	Thr	Leu	Leu	Ile
			100					105					110		
Lys	Thr	Val	Thr	Leu	Val	Leu	Val	Val	Ser	Ser	Gly	Leu	Ser	Leu	Gly
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Lys	Glu	Gly	Pro	Leu	Val	His	Val	Ala	Cys	Cys	Cys	Gly	Asn	Phe	Phe
	130					135					140				
Ser	Ser	Leu	Phe	Ser	Lys	Tyr	Ser	Lys	Asn	Glu	Gly	Lys	Arg	Arg	Glu
145					150					155					160
Val	Leu	Ser	Ala	Ala	Ala	Ala	Ala	Gly	Val	Ser	Val	Ala	Phe	Gly	Ala
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Pro	Ile	Gly	Gly	Val	Leu	Phe	Ser	Leu	Glu	Glu	Val	Ser	Tyr	Tyr	Phe
			180					185					190		
Pro	Leu	Lys	Thr	Leu	Trp	Arg	Ser	Phe	Phe	Ala	Ala	Leu	Val	Ala	Ala
		195					200					205			
Phe	Thr	Leu	Arg	Ser	Ile	Asn	Pro	Phe	Gly	Asn	Ser	Arg	Leu	Val	Leu
	210					215					220				
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225					230					235					240
Phe	Ile	Leu	Leu	Gly	Val	Phe	Gly	Gly	Leu	Trp	Gly	Thr	Leu	Phe	Ile
				245					250					255	
Arg	Cys	Asn	Ile	Ala	Trp	Cys	Arg	Arg	Arg	Lys	Thr	Thr	Arg	Leu	Gly
			260					265					270		
Lys	Tyr	Pro	Val	Leu	Glu	Val	Ile	Val	Val	Thr	Ala	Ile	Thr	Ala	Ile
		275					280					285			
Ile	Ala	Tyr	Pro	Asn	Pro	Tyr	Thr	Arg	Gln	Ser	Thr	Ser	Glu	Leu	Ile
	290					295					300				
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Asn	Phe	Val	Leu	Ser	Ile	Tyr	His	Gly	Asn	Met	Trp	Asp	Leu	Ser	Ser	340	345	350
Pro	Gly	Leu	Ile	Asn	Phe	Gly	Arg	Phe	Asp	Ser	Glu	Lys	Met	Ala	Tyr	355	360	365
Thr	Ile	His	Glu	Ile	Pro	Val	Phe	Ile	Ala	Met	Gly	Val	Val	Gly	Gly	370	375	380
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Arg	Ile	Arg	Tyr	Ile	His	Arg	Pro	Cys	Leu	Gln	Val	Ile	Glu	Ala	Met	405	410	415
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Ser	Arg	Asp	Cys	Gln	Pro	Leu	Gln	Gly	Ser	Ser	Met	Ser	Tyr	Pro	Leu	435	440	445
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Ser	Ile	His	Val	Ser	Gln	Asp	Glu	Arg	Glu	Cys	Thr	Met	Asp	Leu	Ser	725	730	735
Glu	Phe	Met	Asn	Pro	Ser	Pro	Tyr	Thr	Val	Pro	Gln	Glu	Ala	Ser	Leu	740	745	750

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